Effect of Vitamin D Supplementation on Testosterone Levels in Men

S. Pilz1*, S. Frisch2*, H. Koertke2, J. Kuhn3, J. Dreier3, B. Obermayer-Pietsch1, E. Wehr1, A. Zittermann2

1 Department of Internal Medicine, Division of Endocrinology and Metabolism, Medical University of Graz, Austria
2 Clinic for Thoracic and Cardiovascular Surgery, Heart Centre North Rhine-Westphalia, Ruhr University Bochum, Bad Oeynhausen, Germany
3 Institute for Laboratory and Transfusion Medicine, Heart Centre North Rhine-Westphalia, Ruhr University Bochum, Bad Oeynhausen, Germany

Abstract

The male reproductive tract has been identified as a target tissue for vitamin D, and previous data suggest an association of 25-hydroxyvitamin D [25(OH)D] with testosterone levels in men. We therefore aimed to evaluate whether vitamin D supplementation influences testosterone levels in men. Healthy overweight men undergoing a weight reduction program who participated in a randomized controlled trial were analyzed for testosterone levels. The entire study included 200 nondiabetic subjects, of whom 165 participants (54 men) completed the trial. Participants received either 83 μg (3332 IU) vitamin D daily for 1 year (n = 31) or placebo (n = 23). Initial 25(OH)D concentrations were in the deficiency range (<50 nmol/l) and testosterone values were at the lower end of the reference range (9.09–55.28 nmol/l for males aged 20–49 years) in both groups. Mean circulating 25(OH)D concentrations increased significantly by 53.5 nmol/l in the vitamin D group, but remained almost constant in the placebo group. Compared to baseline values, a significant increase in total testosterone levels (from 10.7 ± 3.9 nmol/l to 13.4 ± 4.7 nmol/l, p < 0.001), bioactive testosterone (from 5.21 ± 1.87 nmol/l to 6.25 ± 2.01 nmol/l, p = 0.001), and free testosterone levels (from 0.222 ± 0.080 nmol/l to 0.267 ± 0.087 nmol/l, p = 0.001) were observed in the vitamin D supplemented group. By contrast, there was no significant change in any testosterone measure in the placebo group. Our results suggest that vitamin D supplementation might increase testosterone levels. Further randomized controlled trials are warranted to confirm this hypothesis.

Introduction

Vitamin D deficiency is currently considered an important public health problem being associated with musculoskeletal diseases, cardiovascular disease, cancer, and infectious and autoimmune diseases [1]. The vitamin D receptor (VDR), as well as key enzymes for vitamin D metabolism, are widely expressed in human tissues and cells [2]. In this context, Blomberg Jensen et al. [3] observed significant expressions of the VDR and vitamin D metabolizing enzymes in the male reproductive tract including Leydig cells of the testis. These data raised the question whether vitamin D is able to influence male reproductive hormone production. The existence of such an effect is supported by previous studies suggesting that vitamin D deficiency may contribute to reduced fertility and hypogonadism [2, 3]. These results are of particular interest because both, vitamin D deficiency and hypogonadism are associated with skeletal diseases (e.g., osteoporosis or muscle weakness) as well as extra-skeletal disorders (e.g., cardiovascular disease or obesity) [1, 4, 5]. Recently, some of us [6] have shown in 2,299 men referred for coronary angiography that 25-hydroxyvitamin D [25(OH)D] levels are significantly associated with testosterone levels and that both hormones reveal similar seasonal variations with a peak at the end of summer. Whether there exists a causal link between vitamin D and testosterone status is, however, currently not known. Therefore, a subgroup analysis of a previously published prospective, randomized vitamin D supplementation trial was performed in overweight subjects [7]. Here, we present results on serum testosterone concentrations in the male participants of this study.

*Both authors contributed equally to the present work.
Baseline characteristics of the 54 male patients who completed the trial are shown in Table 1. At study entry, mean 25(OH)D concentrations were in the deficiency range in both groups. During follow-up, weight loss was 5.9 ± 5.3 kg (p = 0.001) in the vitamin D group and 6.6 ± 5.7 kg in the placebo group (p < 0.001), and thus similar in both groups. Circulating 25(OH)D increased by 5.3 ± 65.3 nmol/l to 86.4 ± 68.8 nmol/l in the vitamin D group (p = 0.001), but increased only nonsignificantly in the placebo group (increase by 5.8 ± 21.3 nmol/l to 35.5 ± 18.0 nmol/l; p = 0.215). PTH decreased in the placebo and vitamin D group (decrease by 0.94 ± 3.09; p = 0.035, and 0.60 ± 1.67; p = 0.040, respectively), whereas 1,25(OH)2D tended to increase in both groups (increase by 20.4 ± 41.0; p = 0.027 and 21.7 ± 106.0; p = 0.100, respectively). At baseline, mean testosterone values were at the lower end of the reference range in both groups. By comparing baseline testosterone values with follow-up values in the placebo group no significant change in TT (11.8 ± 4.0 nmol/l vs. 12.7 ± 5.4 nmol/l; p = 0.355), BAT (6.39 ± 2.22 nmol/l vs. 6.59 ± 2.33 nmol/l; p = 0.626) or fT (0.264 ± 0.087 nmol/l vs. 0.278 ± 0.097 nmol/l; p = 0.532) was found. In the vitamin D group, however, a significant increase in all measures of testosterone status was observed. TT increased from 10.7 ± 3.9 nmol/l to 13.4 ± 4.7 nmol/l (p < 0.001), BAT from 5.21 ± 1.87 nmol/l to 6.25 ± 2.01 nmol/l (p = 0.001) and fT from 0.264 ± 0.087 nmol/l to 0.267 ± 0.087 nmol/l (p = 0.001). In the placebo group, there were nonsignificant trends for seasonal differences in 25(OH)D and testosterone values. Compared with men recruited in the summer half-year (mid April to mid October; n = 12), men recruited in the winter half-year (mid October to mid April; n = 11) had lower values of 25(OH)D (21.8 ± 9.8 nmol/l vs. 37.4 ± 30.0 nmol/l;
In overweight men with deficient vitamin D status a significant increase in testosterone was observed after intake of 83 µg vitamin D daily for 1 year whereas there was no significant change in men receiving placebo. This work is, to the best of our knowledge, the first study, which specifically addresses the effect of vitamin D supplementation on androgens in men. The results of this study suggest that vitamin D supplementation might increase testosterone levels in men. Our data support several experimental and clinical findings: First, VDR knockout mice suffer from hypergonadotropic hypogonadism [2]. Second, vitamin D status is directly associated with testosterone levels in men [6]. Third, the male reproductive tract is a target tissue for vitamin D effects [3]. The nonsignificant trend for seasonal differences in both 25(OH)D and testosterone in the placebo group supports our hypothesis of a vitamin D effect on testosterone.

In our study participants, mean baseline 25(OH)D values were in the deficiency range and mean testosterone values were at the lower end of the reference range. Traditionally, low solar ultraviolet B irradiation of the skin is a major cause of vitamin D deficiency [1]. Both, vitamin D [1] and testosterone [5,9] show beneficial effects on the musculoskeletal system. From an evolutionary point of view it would make sense that an active lifestyle (leading to an adequate skin synthesis of vitamin D) also has beneficial effects on muscle function, bone health, and the male reproductive system. We are aware that no final conclusions can be drawn from our study regarding the effect of vitamin D supplementation on testosterone in men but we do believe that our work is of great importance because it provides a reasonable rationale for future studies. Besides the marked increase in 25(OH)D levels in the vitamin D group, there was also a slight (nonsignificant) increase in 25(OH)D in the placebo group during follow-up. We assume that the similar decrease in PTH and the similar trend for an increase in 1,25(OH)2D in both study groups is due to a nonlinear association of these 2 calcitropic hormones with increasing circulating 25(OH)D levels [10], with a pronounced effect at low and virtually no effect at high 25(OH)D levels. Nevertheless, the similar changes in these hormones do not exclude group-specific effects on the reproductive system, since nonclassical target tissues for vitamin D largely depend on circulating 25(OH)D levels [1], which differed markedly between the vitamin D and placebo group.

Our study has both strengths and limitations. Strengths are the study design, the use of a daily vitamin D dose that was effective to increase 25(OH)D values from the deficiency range into the adequate range, and the fact that sample batching was performed to avoid inter-assay variability. One limitation is the fact that the effect of vitamin D supplementation on testosterone was not a prespecified study outcome and that we did not assess testosterone-related functions such as libido, mood, or muscle strength. Another limitation is the relatively small number of male study participants. In addition, future studies have to clarify whether the vitamin D actions are mediated by a pituitary effect or a testicular one.

In conclusion, our study results suggest that vitamin D supplementation might increase testosterone levels in men. Further randomized controlled trials are needed to confirm this hypothesis and to evaluate whether vitamin D driven increases in testosterone levels contribute to the vitamin D effects on various health outcomes.

Acknowledgements

We would like to thank Mrs. Marlen Ewald for excellent technical assistance.

References
6 Wehr E, Pilz S, Boehm BO, Mähr W, Obermayer-Pietsch B. Clin Endocrinol (Oxf) 2010; 73: 243–248